



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**In re Application of:**

Peter ASSAF et al

Serial No.: 10/555,664

Filed: November 04, 2005

**For: NITRIC OXIDE DONORS  
AND USES THEREOF**

Examiner: Sun Jae Y. Loewe

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

## ELECTION

Sir:

This is in response to the United States Patent and Trademark Restriction Office Action mailed October 9, 2007, which response is being made on or before November 9, 2007, and for which no extension of time fee is due.

The Examiner has identified six patentably distinct inventions and has required an election of a single invention under 35 USC § 121 and 372, namely:

Group I - Claims 1-33 and 65-75, drawn to products of Formula I, wherein:

A/X = alkenyl, alkoxy, alkyl, alkynyl, amine, C-amide, carbonyl, C-carboxylate, cycloalkyl, diazo, disulfide, guanidine, guanyl, haloalkyl, hydrazine, N-amide, N-carbamate, nitro, O-carbamate, O-carboxylate, oxygen, sulfur, or absent; cyclic substituents (eg, heteroaryl, aiyl, aryloxy) limited to benzodioxole, diazole, piperidine, pyridine, thiazole, pyrazine, dithiolane, furan, thiophene, benzothiophene, pyrrolidine, quinoline, phenyl, naphthyl.

**B** = unsubstituted alkylene chain or unsubstituted alkylene interrupted by one heteroatom

In re Application of: Peter ASSAF  
 Serial No.: 10/555,664  
 Filed: November 04, 2005  
 Office Action Mailing Date: October 9, 2007

Examiner: Sun Jae Y. Loewe  
 Group Art Unit: 1626  
 Attorney Docket: 30724

B = unsubstituted alkylene chain or unsubstituted alkylene interrupted by one heteroatom

Y = -ONO<sub>2</sub>

Z = hydrogen or unsubstituted alkyl;

Group II - Claims 1-33 and 65-75, drawn to products of Formula I not covered by Group I.

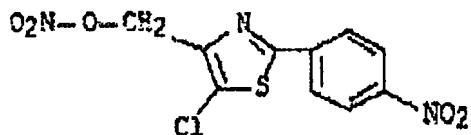
Group III - Claims 34-42, drawn to process of using products of Group I;

Group IV - Claims 34-42, drawn to process of using products of Group II;

Group V - Claims 43-64, drawn to process of making products of Group I;

Group VI - Claims 43-64, drawn to process of making products of Group II;

The Examiner has further stated that the inventions listed in Groups I-VI do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The technical feature linking the subject matter of Groups I-VI is taught in the prior art by Silberg *et al.*, and the prior art compound that anticipates the following Markush alternative of the instant claims:



Applicant wishes to note that the compound recited in Silberg *et al.* is fundamentally different than the compounds taught by the instant application, particularly with regard to the residue formed upon NO release.

The compound taught in Silberg *et al.* has a thiazole ring to which an NO-releasing moiety, -CH<sub>2</sub>-ONO<sub>2</sub>, is attached at the position adjacent to the nitrogen ring atom.

In sharp distinction, in the compounds taught by the instant application, an NO-releasing moiety is attached to the thiazole ring at the position adjacent to the sulfur ring atom.

In re Application of: Peter ASSAF  
 Serial No.: 10/555,664  
 Filed: November 04, 2005  
 Office Action Mailing Date: October 9, 2007

Examiner: Sun Jae Y. Loewe  
 Group Art Unit: 1626  
 Attorney Docket: 30724

As widely discussed in the instant application, the compounds taught therein are designed such that upon releasing NO, a thiamine-derived biocompatible metabolite is produced, thereby reducing the development of tolerance thereto upon repetitive administrations. These compounds were designed while considering the enzymatic mechanisms that lead to the release of bioactive NO, the development of tolerance to NO-donors and the decomposition of Vitamin B<sub>1</sub> (for detailed descriptions see, for example, from page 4 line 16 to page 7 line 2 and from page 29 line 16 to page 30 line 23).

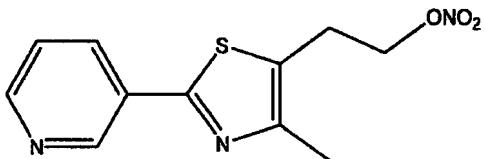
The different structure of the compound taught in Silberg et al. therefore renders this compound structurally and conceptually different from the compounds of the instant application in more than one aspect.

Notwithstanding the above, Applicant hereby elects **Group I, namely Claims 1-33 and 65-75**, drawn to compounds of Formula I and pharmaceutical compositions comprising the same, as defined by the Examiner.

The Examiner has further stated that the application contains Markush claims directed to more than one species and has stated that for Groups II, IV and VI, Applicant is required to elect a single species within the elected group.

It is noted that the Examiner has not required an election of a single species for Group I.

However, in the event the Examiner wishes Applicant to elect a single species within the elected Group I, Applicant hereby selects the compound 3-[4-methyl-5-(2-nitrooxy-ethyl)-thiazole-2-yl]-pyridine (Pet-12), having the following chemical structure:



and corresponding to a compound having Formula 1, wherein:

A is absent;

X is pyridin-3-yl (heteroaryl);

B is ethylene (an unsubstituted alkylene);

In re Application of: Peter ASSAF  
Serial No.: 10/555,664  
Filed: November 04, 2005  
Office Action Mailing Date: October 9, 2007

Examiner: Sun Jae Y. Loewe  
Group Art Unit: 1626  
Attorney Docket: 30724

Y is ONO<sub>2</sub> (NO-releasing group); and  
Z is methyl (unsubstituted alkyl).

Applicant reserves the right to file, at a later date, additional divisional applications claiming priority from the present application which are directed to the non-elected Groups.

Respectfully submitted,

  
Martin D. Moynihan  
Registration No. 40,338

Date: November 06, 2007